General

Guideline Title

Gastro-oesophageal reflux disease: recognition, diagnosis and management in children and young people.

Bibliographic Source(s)

National Collaborating Centre for Women's and Children's Health. Gastro-oesophageal reflux disease: recognition, diagnosis and management in children and young people. London (UK): National Institute for Health and Care Excellence (NICE); 2015 Jan 14. 34 p. (NICE guideline; no. 1).

Guideline Status

This is the current release of the guideline.

This guideline meets NGC's 2013 (revised) inclusion criteria.

Regulatory Alert

FDA Warning/Regulatory Alert

Note from the National Guideline Clearinghouse: This guideline references a drug(s) for which important revised regulatory and/or warning information has been released.

- December 14, 2016 – General anesthetic and sedation drugs : The U.S. Food and Drug Administration (FDA) is warning that repeated or lengthy use of general anesthetic and sedation drugs during surgeries or procedures in children younger than 3 years or in pregnant women during their third trimester may affect the development of children's brains. Consistent with animal studies, recent human studies suggest that a single, relatively short exposure to general anesthetic and sedation drugs in infants or toddlers is unlikely to have negative effects on behavior or learning. However, further research is needed to fully characterize how early life anesthetic exposure affects children's brain development.

Recommendations

Major Recommendations

Note from the National Guideline Clearinghouse (NGC): The guideline was developed by the National Collaborating Centre for Women's and Children's Health on behalf of the National Institute for Health and Care Excellence (NICE). See the "Availability of Companion Documents" field for the full version of this guidance.

The wording used in the recommendations in this guideline (for example, words such as 'offer' and 'consider') denotes the certainty with which the recommendation is made (the strength of the recommendation) and is defined at the end of the "Major Recommendations" field.

Definitions for terms used in the guideline recommendations are detailed in the original guideline document (see the "Availability of Companion Documents" field).

Diagnosing and Investigating Gastro-Oesophageal Reflux Disease (GORD)

Recognise regurgitation of feeds as a common and normal occurrence in infants that:

- Is due to gastro-oesophageal reflux (GOR) – a normal physiological process in infancy
- Does not usually need any investigation or treatment
- Is managed by advising and reassuring parents and carers

Be aware that in a small proportion of infants, GOR may be associated with signs of distress or may lead to certain recognised complications that need clinical management. This is known as gastro-oesophageal reflux disease (GORD).

Give advice about GOR and reassure parents and carers that in well infants, effortless regurgitation of feeds:

- Is very common (it affects at least 40% of infants)
- Usually begins before the infant is 8 weeks old
- May be frequent (5% of those affected have 6 or more episodes each day)
- Usually becomes less frequent with time (it resolves in 90% of affected infants before they are 1 year old)
- Does not usually need further investigation or treatment

When reassuring parents and carers about regurgitation, advise them that they should return for review if any of the following occur:

- The regurgitation becomes persistently projectile
- There is bile-stained (green or yellow-green) vomiting or haematemesis (blood in vomit)
- There are new concerns, such as signs of marked distress, feeding difficulties or faltering growth
- There is persistent, frequent regurgitation beyond the first year of life

In infants, children and young people with vomiting or regurgitation, look out for the 'red flags' in Table 1 in the original guideline document, which may suggest disorders other than GOR. Investigate or refer using clinical judgement.

Do not routinely investigate or treat for GOR if an infant or child without overt regurgitation presents with only one of the following:

- Unexplained feeding difficulties (for example, refusing to feed, gagging or choking)
- Distressed behaviour
- Faltering growth
- Chronic cough
- Hoarseness
- A single episode of pneumonia

Consider referring infants and children with persistent back arching or features of Sandifer's syndrome (episodic torticollis with neck extension and rotation) for specialist assessment.

Recognise the following as possible complications of GOR in infants, children and young people:

- Reflux oesophagitis
- Recurrent aspiration pneumonia
- Frequent otitis media (for example, more than 3 episodes in 6 months)
- Dental erosion in a child or young person with a neurodisability, in particular cerebral palsy

Recognise the following as possible symptoms of GOR in children and young people:

- Heart Burn
- Retrosternal pain
- Epigastric pain

Be aware that GOR is more common in children and young people with asthma, but it has not been shown to cause or worsen it.

Be aware that some symptoms of a non-immunoglobulin E (IgE)-mediated cows' milk protein allergy can be similar to the symptoms of GORD, especially in infants with atopic symptoms, signs and/or family history. If a non-IgE-medicated cows' milk protein allergy is suspected, see the NICE guideline Food allergy in children and young people. Diagnosis and assessment of food allergy in children and young people in primary care and community settings (NICE clinical guideline 116).

When deciding whether to investigate or treat, take into account that the following are associated with an increased prevalence of GORD:

- Premature birth
- Parental history of heartburn or acid regurgitation
- Obesity
- Hiatus hernia
- History of congenital diaphragmatic hernia (repaired)
- History of congenital oesophageal atresia (repaired)
- A neurodisability

GOR only rarely causes episodes of apnoea or apparent life-threatening events (ALTEs), but consider referral for specialist investigations if it is suspected as a possible factor following a general paediatric assessment.

For children and young people who are obese and have heartburn or acid regurgitation, advise them and their parents or carers (as appropriate) that losing weight may improve their symptoms (see also the NGC summary of the NICE guideline Obesity: identification, assessment and management of overweight and obesity in children, young people and adults [NICE clinical guideline 189]).

Do not offer an upper gastrointestinal (GI) contrast study to diagnose or assess the severity of GORD in infants, children and young people.

Perform an urgent (same day) upper GI contrast study for infants with unexplained bile-stained vomiting. Explain to the parents and carers that this is needed to rule out serious disorders such as intestinal obstruction due to mid-gut volvulus.

Consider an upper GI contrast study for children and young people with a history of bile-stained vomiting, particularly if it is persistent or recurrent.

Offer an upper GI contrast study for children and young people with a history of GORD presenting with dysphagia.

Arrange an urgent specialist hospital assessment to take place on the same day for infants younger than 2 months with progressively worsening or forceful vomiting of feeds, to assess them for possible hypertrophic pyloric stenosis.

Arrange a specialist hospital assessment for infants, children and young people for a possible upper GI endoscopy with biopsies if there is:

- Haematemesis (blood-stained vomit) not caused by swallowed blood (assessment to take place on the same day if clinically indicated; see also Table 1 in the original guideline document)
- Melaena (black, foul-smelling stool; assessment to take place on the same day if clinically indicated; see also Table 1 in the original guideline document)
- Dysphagia (assessment to take place on the same day if clinically indicated)
- No improvement in regurgitation after 1 year old
- Persistent, faltering growth associated with overt regurgitation
- Unexplained distress in children and young people with communication difficulties
- Retrosternal, epigastric or upper abdominal pain that needs ongoing medical therapy or is refractory to medical therapy
- Feeding aversion and a history of regurgitation
- Unexplained iron-deficiency anaemia
- A suspected diagnosis of Sandifer's syndrome

Consider performing an oesophageal pH study (or combined oesophageal pH and impedance monitoring if available) in infants, children and young people with:

- Suspected recurrent aspiration pneumonia
- Unexplained apnoeas
- Unexplained non-epileptic seizure-like events
- Unexplained upper airway inflammation
- Dental erosion associated with a neurodisability

- Frequent otitis media
- A possible need for fundoplication (see "Surgery for GORD" below)
- A suspected diagnosis of Sandifer's syndrome

Consider performing an oesophageal pH study without impedance monitoring in infants, children and young people if, using clinical judgement, it is thought necessary to ensure effective acid suppression.

Investigate the possibility of a urinary tract infection in infants with regurgitation if there is:

- Faltering growth
- Late onset (after the infant is 8 weeks old)
- Frequent regurgitation and marked distress

Initial Management of GOR and GORD

Do not use positional management to treat GOR in sleeping infants. In line with National Health Service (NHS) advice , infants should be placed on their back when sleeping.

In breast-fed infants with frequent regurgitation associated with marked distress, ensure that a person with appropriate expertise and training carries out a breastfeeding assessment.

In formula-fed infants with frequent regurgitation associated with marked distress, use the following stepped-care approach:

- Review the feeding history, then
- Reduce the feed volumes only if excessive for the infant's weight, then
- Offer a trial of smaller, more frequent feeds (while maintaining an appropriate total daily amount of milk) unless the feeds are already small and frequent, then
- Offer a trial of thickened formula (for example, containing rice starch, cornstarch, locust bean gum or carob bean gum).

In breast-fed infants with frequent regurgitation associated with marked distress that continues despite a breastfeeding assessment and advice, consider alginate therapy for a trial period of 1 to 2 weeks. If the alginate therapy is successful continue with it, but try stopping it at intervals to see if the infant has recovered.

In formula-fed infants, if the stepped-care approach is unsuccessful (see recommendation above), stop the thickened formula and offer alginate therapy for a trial period of 1 to 2 weeks. If the alginate therapy is successful continue with it, but try stopping it at intervals to see if the infant has recovered.

Pharmacological Treatment of GORD

Do not offer acid-suppressing drugs, such as proton pump inhibitors (PPIs) or H_2 receptor antagonists (H_2RAs), to treat overt regurgitation in infants and children occurring as an isolated symptom.

Consider a 4-week trial of a PPI or H_2RA for those who are unable to tell you about their symptoms (for example, infants and young children, and those with a neurodisability associated with expressive communication difficulties) who have overt regurgitation with 1 or more of the following:

- Unexplained feeding difficulties (for example, refusing feeds, gagging or choking)
- Distressed behaviour
- Faltering growth

Consider a 4-week trial of a PPI or H_2RA for children and young people with persistent heartburn, retrosternal or epigastric pain.

Assess the response to the 4-week trial of the PPI or H_2RA, and consider referral to a specialist for possible endoscopy if the symptoms:

- Do not resolve or
- Recur after stopping the treatment

When choosing between PPIs and H_2RAs, take into account:

- The availability of age-appropriate preparations
- The preference of the parent (or carer), child or young person (as appropriate)

- Local procurement costs

Offer PPI or H_2RA treatment to infants, children and young people with endoscopy-proven reflux oesophagitis, and consider repeat endoscopic examinations as necessary to guide subsequent treatment.

Do not offer metoclopramide, domperidone or erythromycin to treat GOR or GORD without seeking specialist advice and taking into account their potential to cause adverse events.

Enteral Tube Feeding for GORD

Only consider enteral tube feeding to promote weight gain in infants and children with overt regurgitation and faltering growth if:

- Other explanations for poor weight gain have been explored and/or
- Recommended feeding and medical management of overt regurgitation is unsuccessful

Before starting enteral tube feeding for infants and children with faltering growth associated with overt regurgitation, agree in advance:

- A specific, individualised nutrition plan
- A strategy to reduce it as soon as possible
- An exit strategy, if appropriate, to stop it as soon as possible

In infants and children receiving enteral tube feeding for faltering growth associated with overt regurgitation:

- Provide oral stimulation, continuing oral feeding as tolerated
- Follow the nutrition plan, ensuring that the intended target weight is achieved and that appropriate weight gain is sustained
- Reduce and stop enteral tube feeding as soon as possible

Consider jejunal feeding for infants, children and young people:

- Who need enteral tube feeding but who cannot tolerate intragastric feeds because of regurgitation or
- If reflux-related pulmonary aspiration is a concern

Surgery for GORD

Offer an upper GI endoscopy with oesophageal biopsies for infants, children and young people before deciding whether to offer fundoplication for presumed GORD.

Consider performing other investigations such as an oesophageal pH study (or combined oesophageal pH and impedance monitoring if available) and an upper GI contrast study for infants, children and young people before deciding whether to offer fundoplication.

Consider fundoplication in infants, children and young people with severe, intractable GORD if:

- Appropriate medical treatment has been unsuccessful or
- Feeding regimens to manage GORD prove impractical, for example, in the case of long-term, continuous, thickened enteral tube feeding.

Definitions:

Strength of Recommendations

Some recommendations can be made with more certainty than others. The Guideline Development Group (GDG) makes a recommendation based on the trade-off between the benefits and harms of an intervention, taking into account the quality of the underpinning evidence. For some interventions, the GDG is confident that, given the information it has looked at, most patients would choose the intervention. The wording used in the recommendations in this guideline denotes the certainty with which the recommendation is made (the strength of the recommendation).

Interventions That Must (or Must Not) Be Used

The GDG usually uses 'must' or 'must not' only if there is a legal duty to apply the recommendation. Occasionally 'must' (or 'must not') is used if the consequences of not following the recommendation could be extremely serious or potentially life threatening.

Interventions That Should (or Should Not) Be Used – a 'Strong' Recommendation

The GDG uses 'offer' (and similar words such as 'refer' or 'advise') when confident that, for the vast majority of patients, an intervention will do

more good than harm, and be cost effective. Similar forms of words (for example, 'Do not offer…') are used when the GDG is confident that an intervention will not be of benefit for most patients.

Interventions That Could Be Used

The GDG uses 'consider' when confident that an intervention will do more good than harm for most patients, and be cost effective, but other options may be similarly cost effective. The choice of intervention, and whether or not to have the intervention at all, is more likely to depend on the patient's values and preferences than for a strong recommendation, and so the healthcare professional should spend more time considering and discussing the options with the patient.

Clinical Algorithm(s)

A National Institute for Health and Care Excellence (NICE) care pathway titled "Dyspepsia and Gastro-oesophageal Reflux Disease Overview" is available from the NICE Web site .

Scope

Disease/Condition(s)

- Gastro-oesophageal reflux (GOR)
- Gastro-oesophageal reflux disease (GORD)

Guideline Category

Diagnosis

Evaluation

Management

Treatment

Clinical Specialty

Family Practice

Gastroenterology

Neurology

Nursing

Nutrition

Pediatrics

Surgery

Intended Users

Advanced Practice Nurses

Dietitians

Nurses

Physician Assistants

Physicians

Guideline Objective(s)

To produce a clinical guideline on the investigation and management of gastro-oesophageal reflux disease (GORD) in children

Target Population

Infants, children and young people under 18 years with symptoms of gastro-oesophageal reflux (GOR), with specific consideration given to children and young people with neurodevelopmental disorders

Note: The following groups were excluded from the guideline:

- People ages 18 years and older
- Children and young people with Barrett's oesophagus
- Reflux associated with pregnancy

Interventions and Practices Considered

Diagnosis/Evaluation

1. Assessing signs and symptoms of gastro-esophageal reflux (GOR)
2. Providing advice and reassurance to parents and carers
3. Recognising "red flag" symptoms that may require additional investigation or specialty referral
4. Upper gastrointestinal (GI) contrast study
5. Urgent specialist hospital assessment if indicated
6. Upper GI endoscopy
7. Oesophageal pH study (or combined oesophageal pH and impedance monitoring)
8. Investigating possibility of urinary tract infection

Management/Treatment

1. Positional management (not recommended)
2. Breastfeeding assessment
3. Feeding history and adjustment of feeding volumes and frequency
4. Trial of thickened formula
5. Alginate therapy
6. Pharmacological treatment
    - Proton pump inhibitors (PPIs)
    - H_2 receptor antagonists (H_2RA)
    - Metoclopramide, domperidone or erythromycin (not recommended without seeking specialist advice)
7. Enteral tube feeding
8. Surgical fundoplication

Major Outcomes Considered

- Health-related quality of life
- Change in symptoms and signs, for example:
    - Cessation or reduction (volume or frequency) of regurgitation
    - Deduction in crying and distress
    - Improved feeding
    - Improved nutritional status

- Improvement in investigative findings, including healing of erosive oesophagitis
- Adverse events of interventions (diagnostic or treatment)
- Resource use and cost

Methodology

Methods Used to Collect/Select the Evidence

Searches of Electronic Databases

Description of Methods Used to Collect/Select the Evidence

Note from the National Guideline Clearinghouse (NGC): The guideline was developed by the National Collaborating Centre for Women's and Children's Health on behalf of the National Institute for Health and Care Excellence (NICE). See the "Availability of Companion Documents" field for the full version of this guidance.

Developing Review Questions and Protocols and Identifying Evidence

The scope for this guideline (see Appendix B in the full version of the guideline [see the "Availability of Companion Documents" field]) outlines the main areas where guidance is needed. The guideline development group formulated review questions based on the scope and prepared a protocol for each review question (see Appendix E in the full version of the guideline). These formed the starting point for systematic reviews of relevant evidence. Published evidence was identified by applying systematic search strategies (see Appendix F in the full version of the guideline) to the following databases: Medline (1948 onwards), EMBASE (1980 onwards), 4 Cochrane databases (Cochrane Central Register of Controlled Trials, Cochrane Database of Systematic Reviews, the Database of Abstracts of Reviews of Effects and the Health Technology Assessment [HTA] database). Searches to identify economic studies were undertaken using the above databases and the National Health Service Economic Evaluation Database (NHS EED). Where possible, search strategies were restricted to English language. If this was not possible, studies in languages other than English were not reviewed. Search filters were used to identify particular study designs, such as randomised controlled trials (RCTs). There was no searching of grey literature, nor was hand searching of journals undertaken.

All the searches were updated and re-executed within 6 to 8 weeks of the start of the stakeholder consultation to ensure the reviews were up-to-date. This process was completed by April 2014.

GER and GERD are equivalent acronyms to GOR and GORD that reflect the American English spelling of oesophagus as esophagus. GER and GERD were included in the search strategies.

Outcome Measures

For this guideline, the review questions were judged on a number of outcomes. The justification for using these outcomes was based on their relevance to the groups covered by the guideline and consensus among members of the guideline development group. The guideline development group selected 7 or 8 outcomes for each review when assessing the effectiveness of a particular treatment. No further distinction was made with regard to whether each was critical or important to the guideline development group's decision-making. Outcomes included those that were felt to be desirable (for example reduction in overt regurgitation) and unwanted effects of treatment that it would be important to reduce to a minimum.

Incorporating Health Economics

The aims of the health economic input to the guideline were to inform the guideline development group of new economic issues relating to reflux in children and young people, and to consider whether the recommendations continued to represent a cost-effective use of healthcare resources. Health economic evaluations aim to integrate data on benefits (ideally in terms of quality adjusted life years [QALYs]), harms and costs of different care options.

Systematic searches for published economic evidence were undertaken for all clinical questions in the guideline.

The guideline development group prioritised a number of clinical questions where it was thought that economic considerations would be particularly important in formulating recommendations. For this guideline the areas prioritised for economic analysis were:

- Antacids/alginates

- H_2-receptor antagonists
- Proton pump inhibitors
- Prokinetic agents
- Enteral tube feeding
- Fundoplication surgery

A systematic search for published economic evidence was undertaken for these questions. Due to the limited evidence on the effectiveness of managing gastro-oesophageal reflux disease (GORD) in children, economic analysis was restricted to costs and resource use of each of the management approaches.

A detailed review of Health Economics can be found in Appendix A in the full version of the guideline.

Number of Source Documents

See Appendix G, "Summary of Identified Studies," in the full version of the guideline (see the "Availability of Companion Documents" field) for a detailed breakdown of the total number of papers identified, duplicates removed, papers weeded out, papers abandoned, papers excluded, and papers included for each protocol question, two-stage review question, and scope question.

Methods Used to Assess the Quality and Strength of the Evidence

Weighting According to a Rating Scheme (Scheme Given)

Rating Scheme for the Strength of the Evidence

Overall Quality of Outcome Evidence in Grading of Recommendations Assessment, Development and Evaluation (GRADE)

Level	Description
High	Further research is very unlikely to change confidence in the estimate of effect.
Moderate	Further research is likely to have an important impact on confidence in the estimate of effect and may change the estimate.
Low	Further research is very likely to have an important impact on confidence in the estimate of effect and is likely to change the estimate.
Very Low	Any estimate of effect is very uncertain.

Methods Used to Analyze the Evidence

Meta-Analysis

Review of Published Meta-Analyses

Systematic Review with Evidence Tables

Description of the Methods Used to Analyze the Evidence

Note from the National Guideline Clearinghouse (NGC): The guideline was developed by the National Collaborating Centre for Women's and Children's Health on behalf of the National Institute for Health and Care Excellence (NICE). See the "Availability of Companion Documents" field for the full version of this guidance.

Reviewing and Synthesising Evidence

Evidence relating to clinical effectiveness was reviewed and synthesised according to the Grading of Recommendations Assessment, Development and Evaluation (GRADE) approach. In the GRADE approach, the quality of the evidence identified for each outcome listed in the review protocol is assessed according to the factors listed below and an overall quality rating (high, moderate, low or very low) is assigned by combining the ratings

for the individual factors.

- Study design (as an indicator of intrinsic bias; this determines the initial quality rating)
- Limitations in the design or execution of the study (including concealment of allocation, blinding, loss to follow up; these can reduce the quality rating)
- Inconsistency of effects across studies (this can reduce the quality rating)
- Indirectness (the extent to which the available evidence fails to address the specific review question; this can reduce the quality rating)
- Imprecision (reflects the confidence in the estimate of effect and this can reduce the quality rating). For continuous variables (such as change in temperature) the guideline development group was asked to predefine minimally important differences (the smallest difference between treatments that healthcare professionals or patients think is clinically beneficial). However, the guideline development group was unable to agree these, so imprecision was graded based on the GRADE default for risk ratios and odds ratios of −0.75/1.25 and for continuous outcomes of SMD±0.5.
- Other considerations (including large magnitude of effect, evidence of a dose–response relationship, or confounding variables likely to have reduced the magnitude of an effect; these can increase the quality rating in observational studies, provided no downgrading for other features has occurred)

For each review question the highest available level of evidence was sought. The type of review question determines the highest level of evidence. For questions on therapy or treatment, the highest possible evidence level is a well-conducted systematic review or meta-analysis of randomised controlled trials (RCTs), or an individual RCT. In the GRADE approach, a body of evidence based entirely on such studies has an initial quality rating of high, and this may be downgraded to moderate, low or very low if factors listed above are not addressed adequately. For questions on prognosis, the highest possible level of evidence is a controlled observational study (a cohort study or case–control study), and a body of evidence based on such studies would have an initial quality rating of high, which might be downgraded to moderate, low or very low, depending on the factors listed above. For diagnostic tests, studies examining the performance of the test started as high quality if information on accuracy was required, but where an evaluation of the effectiveness of the test in the clinical management of the condition was required, evidence from RCTs or cohort studies was considered optimal.

Where appropriate, the body of evidence corresponding to each outcome specified in the review protocol was subjected to quantitative meta-analysis. In such cases, pooled effect sizes were presented as pooled risk ratios (RRs), pooled odds ratios (ORs) or weighted mean differences. By default, meta-analyses were conducted by fitting fixed effects models, but where statistically significant heterogeneity was identified, random effects models were used to investigate the impact of the heterogeneity. Where quantitative meta-analysis could not be undertaken (for example because of heterogeneity in the included studies) the range of effect sizes reported in the included studies was presented. The GRADE profiles are not directly applicable to epidemiological studies or non-comparative cohort studies. Where these studies are presented, they are included in descriptive paragraphs and/or tables as appropriate.

For studies evaluating the accuracy of a diagnostic test, summary statistics (sensitivity, specificity, positive predictive value [PPV], negative predictive value [NPV] and likelihood ratios for positive and negative test results [LR+ and LR−, respectively]) were calculated or quoted where possible (see Table 4 in the full version of the guideline). The following definitions were used when summarising the likelihood ratios for the guideline development group:

- Convincing: positive likelihood ratio (LR+) 10 or higher, negative likelihood ratio (LR−) 0.1 or lower
- Strong: LR+ 5 or higher (but less than 10), LR− 0.2 or lower (but higher than 0.1)
- Not strong: LR+ 4.9 or lower, LR− higher than 0.2

The following definitions were used when summarising the levels of sensitivity, specificity, positive predictive value (PPV) and negative predictive value (NPV) for the guideline development group:

- High: 90% and above
- Moderate: 75% to 89%
- Low: 74% or below

Particular emphasis was placed on the positive likelihood ratio, with a ratio of 5 or higher being considered a good indicator that a symptom or sign should be used.

Some studies were excluded from the guideline reviews after obtaining copies of the publications because they did not meet inclusion criteria specified by the guideline development group (see Appendix H in the full version of the guideline). The characteristics of each included study were summarised in evidence tables for each review question (see Appendix I of the full version of the guideline). Where possible, dichotomous outcomes were presented as relative risks (RRs) or ORs with 95% confidence intervals (CIs), and continuous outcomes were presented as mean

differences with 95% CIs or standard deviations (SDs).

Incorporating Health Economics Evidence

For economic evaluations, no standard system of grading the quality of evidence exists and included papers were assessed using a quality assessment checklist based on good practice in economic evaluation. Reviews of the relevant published health economic literature identified in the literature search are presented alongside the clinical effectiveness reviews in the full version of the guideline.

A detailed review of health economics can be found in Appendix A in the full version of the guideline.

Methods Used to Formulate the Recommendations

Expert Consensus (Nominal Group Technique)

Informal Consensus

Description of Methods Used to Formulate the Recommendations

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Who Has Developed the Guideline

The guideline was developed by a multi-professional and lay working group (the guideline development group) convened by the National Collaborating Centre for Women's and Children's Health (NCC-WCH). Membership included two consultant paediatric gastroenterologists, two consultant paediatricians, one consultant in paediatric neurodisability, one paediatric surgeon, two general practitioners, one advanced paediatric nurse practitioner, one paediatric dietician, one health visitor and two patient/carer/consumer representatives.

Staff from the NCC-WCH provided methodological support for the guideline development process, undertook systematic searches, retrieval and appraisal of the evidence, and health economics modelling.

Guideline Development Methodology

This guideline was commissioned by NICE and developed in accordance with the guideline development process outlined in The Guideline Development Process – Information for National Collaborating Centres and Guideline Development Groups (available from the www.nice.org.uk).

In accordance with NICE's Equality Scheme, ethnic and cultural considerations and factors relating to disabilities have been considered by the guideline development group throughout the development process and specifically addressed in individual recommendations where relevant. For further information, see the NICE Equality Scheme .

Evidence to Recommendations

Recommendations for clinical care were derived using, and linked explicitly to, the evidence that supported them. In the first instance, informal consensus methods were used by the guideline development group to agree short clinical and, where appropriate, cost effectiveness evidence statements which were presented alongside the evidence profiles. Statements summarising the guideline development group' interpretation of the evidence and any extrapolation from the evidence used when making recommendations were also written to ensure transparency in the decision-making process. The criteria used in moving from evidence to recommendations were:

- Relative value placed on the outcomes considered
- Consideration of clinical benefits and harms consideration of net health benefits and resource use
- Quality of the evidence
- Other considerations (including equalities issues)

The guideline development group also identified areas where evidence to answer its review questions was lacking and used this information to formulate recommendations for future research.

Towards the end of the guideline development process, formal consensus methods were used to consider all the clinical care recommendations and research recommendations that had been drafted. The guideline development group identified 9 "key priorities for implementation" (key recommendations) and 3 high priority research recommendations. The key priorities for implementation were those recommendations thought likely to have the greatest impact on clinical care and outcomes in the Nation Health Service (NHS) as a whole; they were selected using a variant of the nominal group technique (see the NICE guidelines manual 2012 [see the "Availability of Companion Documents" field]). The priority research recommendations were selected in a similar way.

Rating Scheme for the Strength of the Recommendations

Strength of Recommendations

Some recommendations can be made with more certainty than others. The Guideline Development Group (GDG) makes a recommendation based on the trade-off between the benefits and harms of an intervention, taking into account the quality of the underpinning evidence. For some interventions, the GDG is confident that, given the information it has looked at, most patients would choose the intervention. The wording used in the recommendations in this guideline denotes the certainty with which the recommendation is made (the strength of the recommendation).

Interventions That Must (or Must Not) Be Used

The GDG usually uses 'must' or 'must not' only if there is a legal duty to apply the recommendation. Occasionally 'must' (or 'must not') is used if the consequences of not following the recommendation could be extremely serious or potentially life threatening.

Interventions That Should (or Should Not) Be Used – a 'Strong' Recommendation

The GDG uses 'offer' (and similar words such as 'refer' or 'advise') when confident that, for the vast majority of patients, an intervention will do more good than harm, and be cost effective. Similar forms of words (for example, 'Do not offer…') are used when the GDG is confident that an intervention will not be of benefit for most patients.

Interventions That Could Be Used

The GDG uses 'consider' when confident that an intervention will do more good than harm for most patients, and be cost effective, but other options may be similarly cost effective. The choice of intervention, and whether or not to have the intervention at all, is more likely to depend on the patient's values and preferences than for a strong recommendation, and so the healthcare professional should spend more time considering and discussing the options with the patient.

Cost Analysis

A detailed review of Health Economics can be found in Appendix A of the full version of the guideline (see the "Availability of Companion Documents" field). For almost all the interventions considered in this guideline, published evidence of cost effectiveness was lacking. Further analysis was undertaken to support the guideline development group's decision making where health economic input was recognised as useful. None of the analyses presented in Appendix A follow the National Institute for Health and Care Excellence's (NICE's) reference case for health economic analysis because of the lack of evidence for effectiveness.

In all topics considered for economic evaluation, resource use and costs were quantified. Details of the methods used in relation to each review question are presented in Appendix A. For each question the following are reported: review of published economic literature; description of resource use and costs; and conclusions of the analysis.

For each review question considered in the guideline, Appendix A includes a summary based on evidence and the opinions of the guideline development group.

Relevant health economic evidence for recommendations can also be found in the specific chapters in the full version of the guideline.

Method of Guideline Validation

External Peer Review

Internal Peer Review

Description of Method of Guideline Validation

Stakeholder Involvement

Registered stakeholder organisations were invited to comment on the draft scope and the draft guideline. The guideline development group carefully considered and responded to all comments received from stakeholder organisations. The comments and responses were reviewed by National Institute for Health and Care Excellence (NICE) in accordance with the NICE guideline development process (see the NICE guidelines manual 2012 [see the "Availability of Companion Documents" field]).

Evidence Supporting the Recommendations

Type of Evidence Supporting the Recommendations

The type of evidence supporting the recommendations is not specifically stated.

The type and quality of evidence supporting each review question are described in evidence profiles in the full version of the guideline (see the "Availability of Companion Documents" field).

Benefits/Harms of Implementing the Guideline Recommendations

Potential Benefits

Appropriate diagnosis and management of children and young people with gastro-oesophageal reflux disease (GORD)

Refer to the "Consideration of clinical benefits and harms" sections in the full version of the guideline (see the "Availability of Companion Documents" field) for benefits of specific interventions.

Potential Harms

- A false positive diagnosis of gastro-oesophageal reflux disease (GORD) could potentially have adverse consequences, including unnecessary investigations, such as endoscopy, or the use of unnecessary treatments. Endoscopy is usually performed under sedation or more frequently under general anesthesia in children and there are small associated risks. Oesophageal pH monitoring can be a somewhat distressing investigation, requiring placement of a naso-oesophogeal probe. Unnecessary treatment with drugs such as acid suppressing agents (such as proton pump inhibitors [PPIs] or H_2 receptor antagonists [H_2RAs]) is not high risk but nevertheless undesirable.

  Conversely, false negative clinical evaluation could result in delayed investigation or treatment. Avoidance of unnecessary radiation exposure was seen by the group as a very important priority.
- The group discussed the practicalities of using feed thickeners. They noted that there are number of feed thickening products available; both on prescription and over the counter. These products vary across commercial brands but are basically either pre-thickened formulae or products added to formula milk. The group was aware that both types of thickened feeds are associated with difficulties in achieving a successful feed, with reported resistance to the texture from the child and the increased viscosity effecting the feeding time. However, these difficulties did not outweigh the benefits of reducing reflux.
- Acid suppressing agents, such as H_2RAs and PPIs, are generally well tolerated but do have potential side effects. Long-term acid suppression might have adverse consequences. Acid, for example, has a protective effect against bacterial gastrointestinal infection and studies have shown an increased incidence of salmonella infection in people using such agents. It is important, therefore, that widespread unnecessary usage be avoided, and that where these drugs are used, unnecessarily long-term usage be avoided. Other agents, such as metoclopramide and domperidone, which act as pro-kinetic agents do have significant associated adverse effects, such as neurological symptoms (dyskinetic effects). There are concerns with domperidone regarding potential dysrrhythmias. The group was therefore concerned that these should only be considered for use following specialist advice.
- It was the experience of the group that feeding exclusively via an enteral tube can create behavioural issues relating to oral food aversion when tube feeding is stopped. Enteral tube feeding can disrupt normal feeding behaviour and therefore can lead to long-term feeding difficulties. It was agreed that as a precautionary measure, oral stimulation should be continued throughout enteral tube feeding treatment.

Dependent on the individual, the group felt a variety of tastes and textures should be explored. It was outlined by the group that using enteral tube feeding in children with faltering growth can result in the child receiving a quantity of feed that they had not previously been used to, and that this could potentially cause reflux. The group concluded that in the first instance the quantity and timing of feeding should be monitored to avoid this, as per the guideline recommendation for formula feeding.

- The GDG recognised certain circumstances in which jejunal feeding might be preferable to providing intra-gastric tube feeds. In some infants, children and young people receiving intra-gastric feeding, GOR may continue to be a significant concern to the degree that they are not able to tolerate it, resulting, for example, in very frequent overt regurgitation. Also, there are circumstances in which it is judged that reflux is associated with a high risk of pulmonary aspiration. By delivering the feed into the jejunum, the risk of reflux may be significantly less. The group recognised that placement of jejunal tubes can be difficult and displacement of such tubes may pose problems. This was not, therefore, a procedure to be undertaken unless there were clear indications.
- As with any invasive intervention, the benefits, risks and potential complications of fundoplication must be weighed up very carefully. The operation is performed relatively frequently, but there are several potential complications. The creation of the high pressure zone in the oesophagus will cause dysphagia (difficulty in swallowing), particularly of solid foods. Typically, this symptom will resolve over the first 6 months after the procedure, but a restricted diet may initially be required. Frequently, children are unable to burp following the procedure. This leads to episodes of stomach distension, causing discomfort, particularly in relation to feeds. This is termed 'gas bloat'. While this symptom also tends to improve with time, it can be a cause of marked distress. Retching can be an intractable symptom following fundoplication, particularly in neurologically impaired children, although it is not possible to accurately predict prior to surgery which children will be most troubled by this symptom.

Refer to the "Consideration of clinical benefits and harms" sections in the full version of the guideline (see the "Availability of Companion Documents" field) for additional discussion of harms of specific interventions.

Qualifying Statements

Qualifying Statements

- This guidance represents the view of the National Institute for Health and Care Excellence (NICE), which was arrived at after careful consideration of the evidence available. Healthcare professionals are expected to take it fully into account when exercising their clinical judgement. However, the guidance does not override the individual responsibility of healthcare professionals to make decisions appropriate to the circumstances of the individual patient, in consultation with the patient and/or guardian or carer, and informed by the summaries of product characteristics of any drugs.
- Implementation of this guidance is the responsibility of local commissioners and/or providers. Commissioners and providers are reminded that it is their responsibility to implement the guidance, in their local context, in light of their duties to have due regard to the need to eliminate unlawful discrimination, advance equality of opportunity and foster good relations. Nothing in this guidance should be interpreted in a way that would be inconsistent with compliance with those duties.
- Remember that child maltreatment is common, can present anywhere, and may co-exist with other health problems, including gastro-oesophageal reflux disease (GORD). For more information, see the NICE guideline on child maltreatment.
- The guideline will assume that prescribers will use a medicine's summary of product characteristics to inform decisions made with individual patients.
- Treatment and care should take into account individual needs and preferences. Patients should have the opportunity to make informed decisions about their care and treatment, in partnership with their healthcare professionals. If the patient is under 16, their family or carers should also be given information and support to help the child or young person to make decisions about their treatment. Healthcare professionals should follow the Department of Health's advice on consent. If someone does not have capacity to make decisions, healthcare professionals should follow the code of practice that accompanies the Mental Capacity Act and the supplementary code of practice on deprivation of liberty safeguards.
- If a young person is moving between paediatric and adult services, care should be planned and managed according to the best practice guidance described in the Department of Health's Transition: getting it right for young people.
- Adult and paediatric healthcare teams should work jointly to provide assessment and services to young people with GORD. Diagnosis and management should be reviewed throughout the transition process, and there should be clarity about who is the lead clinician to ensure continuity of care.
- For all recommendations, NICE expects that there is discussion with the patient about the risks and benefits of the interventions, and their values and preferences. This discussion aims to help them to reach a fully informed decision.

Implementation of the Guideline

Description of Implementation Strategy

Implementation tools and resources to help clinicians put the guideline into practice are also available on the National Institute for Health and Care Excellence (NICE) Web site (see also the "Availability of Companion Documents" field).

Key Priorities for Implementation

The following recommendations have been identified as priorities for implementation.

Give advice about gastro-oesophageal reflux (GOR) and reassure parents and carers that in well infants, effortless regurgitation of feeds:

- Is very common (it affects at least 40% of infants)
- Usually begins before the infant is 8 weeks old
- May be frequent (5% of those affected have 6 or more episodes each day)
- Usually becomes less frequent with time (it resolves in 90% of affected infants before they are 1 year old)
- Does not usually need further investigation or treatment

In infants, children and young people with vomiting or regurgitation, look out for the 'red flags' in table 1 in the original guideline document, which may suggest disorders other than GOR. Investigate or refer using clinical judgement.

Do not routinely investigate or treat for GOR if an infant or child without overt regurgitation presents with only 1 of the following:

- Unexplained feeding difficulties (for example, refusing to feed, gagging or choking)
- Distressed behaviour
- Faltering growth
- Chronic cough
- Hoarseness
- A single episode of pneumonia

Do not offer an upper gastrointestinal (GI) contrast study to diagnose or assess the severity of gastrointestinal reflux disease (GORD) in infants, children and young people.

Arrange a specialist hospital assessment for infants, children and young people for a possible upper GI endoscopy with biopsies if there is:

- Haematemesis (blood-stained vomit) not caused by swallowed blood (assessment to take place on the same day if clinically indicated; also see table 1 in the original guideline document)
- Melaena (black, foul-smelling stool; assessment to take place on the same day if clinically indicated; also see table 1 in the original guideline document)
- Dysphagia (assessment to take place on the same day if clinically indicated)
- No improvement in regurgitation after 1 year old
- Persistent, faltering growth associated with overt regurgitation
- Unexplained distress in children and young people with communication difficulties
- Retrosternal, epigastric or upper abdominal pain that needs ongoing medical therapy or is refractory to medical therapy
- Feeding aversion and a history of regurgitation
- Unexplained iron-deficiency anaemia
- A suspected diagnosis of Sandifer's syndrome

In formula-fed infants with frequent regurgitation associated with marked distress, use the following stepped-care approach:

- Review the feeding history, then
- Reduce the feed volumes only if excessive for the infant's weight, then
- Offer a trial of smaller, more frequent feeds (while maintaining an appropriate total daily amount of milk) unless the feeds are already small and frequent, then
- Offer a trial of thickened formula (for example, containing rice starch, cornstarch, locust bean gum or carob bean gum)

In formula-fed infants, if the stepped-care approach is unsuccessful, stop the thickened formula and offer alginate therapy for a trial period of 1 to

2 weeks. If the alginate therapy is successful continue with it, but try stopping it at intervals to see if the infant has recovered.

Do not offer acid-suppressing drugs, such as proton pump inhibitors (PPIs) or H_2 receptor antagonists (H_2RAs), to treat overt regurgitation in infants and children occurring as an isolated symptom.

Do not offer metoclopramide, domperidone or erythromycin to treat GOR or GORD without seeking specialist advice and taking into account their potential to cause adverse events.

Implementation Tools

Clinical Algorithm

Mobile Device Resources

Patient Resources

Resources

For information about availability, see the *Availability of Companion Documents* and *Patient Resources* fields below.

Institute of Medicine (IOM) National Healthcare Quality Report Categories

IOM Care Need

Getting Better

Living with Illness

IOM Domain

Effectiveness

Patient-centeredness

Identifying Information and Availability

Bibliographic Source(s)

National Collaborating Centre for Women's and Children's Health. Gastro-oesophageal reflux disease: recognition, diagnosis and management in children and young people. London (UK): National Institute for Health and Care Excellence (NICE); 2015 Jan 14. 34 p. (NICE guideline; no. 1).

Adaptation

Not applicable: The guideline was not adapted from another source.

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Financial Disclosures/Conflicts of Interest

All guideline development group members' interests were recorded on declaration forms provided by the National Institute for Health and Care Excellence (NICE). The form covered consultancies, fee-paid work, shareholdings, fellowships and support from the healthcare industry.

See Section 4.5 in the original guideline document for a list of declarations. All other members of the group stated that they had no interests to declare.

Guideline Status

This is the current release of the guideline.

This guideline meets NGC's 2013 (revised) inclusion criteria.

Guideline Availability

Electronic copies: Available from the National Institute for Health and Care Excellence (NICE) Web site . Also available for download in ePub and eBook formats from the NICE Web site .

Availability of Companion Documents

The following are available:

- Gastro-oesophageal reflux disease: recognition, diagnosis and management in children and young people. Full guideline. London (UK): National Institute for Health and Care Excellence (NICE); 2015 Jan. 218 p. (NICE guideline; no. 1). Electronic copies: Available from the National Institute for Health and Care Excellence (NICE) Web site .

- Gastro-oesophageal reflux disease: recognition, diagnosis and management in children and young people. Appendices A-E, G-H, J. London (UK): National Institute for Health and Care Excellence (NICE); 2015 Jan. 66 p. (NICE guideline; no. 1) Electronic copies: Available from the NICE Web site .
- Gastro-oesophageal reflux disease: recognition, diagnosis and management in children and young people. Appendix I: evidence tables. London (UK): National Institute for Health and Care Excellence (NICE); 2015 Jan. 243 p. (NICE guideline; no. 1) Electronic copies: Available from the NICE Web site .
- Gastro-oesophageal reflux disease: recognition, diagnosis and management in children and young people. GORD search strategies. London (UK): National Institute for Health and Care Excellence (NICE); 2015 Jan. 125 p. (NICE guideline; no. 1). Electronic copies: Available from the NICE Web site .
- Gastro-oesophageal reflux disease: recognition, diagnosis and management in children and young people. Costing statement. London (UK): National Institute for Health and Care Excellence; 2015 Jan. 8 p. (NICE guideline; no. 1). Electronic copies: Available from the NICE Web site .
- Gastro-oesophageal reflux disease: recognition, diagnosis and management in children and young people. Baseline assessment tool. London (UK): National Institute for Health and Care Excellence; 2015 Jan. (NICE guideline; no. 1). Electronic copies: Available from the NICE Web site .
- Gastro-oesophageal reflux disease: recognition, diagnosis and management in children and young people. Clinical audit tool. London (UK): National Institute for Health and Care Excellence; 2015 Jan. (NICE guideline; no. 1). Electronic copies: Available from the NICE Web site .
- The guidelines manual 2012. London (UK): National Institute for Health and Care Excellence (NICE); 2012 Nov. Electronic copies: Available from the NICE Web site .

Patient Resources

The following is available:

- Gastro-oesophageal reflux disease: recognition, diagnosis and management in children and young people. Information for the public. London (UK): National Institute for Health and Care Excellence; 2015 Jan. 10 p. (NICE guideline; no. 1). Electronic copies: Available from the National Institute for Health and Care Excellence (NICE) Web site . Also available for download in ePub and eBook formats from the NICE Web site . Also available in Welsh from the NICE Web site .

Please note: This patient information is intended to provide health professionals with information to share with their patients to help them better understand their health and their diagnosed disorders. By providing access to this patient information, it is not the intention of NGC to provide specific medical advice for particular patients. Rather we urge patients and their representatives to review this material and then to consult with a licensed health professional for evaluation of treatment options suitable for them as well as for diagnosis and answers to their personal medical questions. This patient information has been derived and prepared from a guideline for health care professionals included on NGC by the authors or publishers of that original guideline. The patient information is not reviewed by NGC to establish whether or not it accurately reflects the original guideline's content.

NGC Status

This NGC summary was completed by ECRI Institute on March 12, 2015. This summary was updated by ECRI Institute on February 15, 2017 following the U.S. Food and Drug Administration advisory on general anesthetic and sedation drugs.

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